REMARKS

Status Summary

Claims 1-31 were pending in the present application. Applicants have cancelled claims 9, 10, 16, 17, and 25-31. As such, claims 1-8, 11-15 and 18-24 are currently pending.

The Patent Office has rejected claims 1-8, 12-15, 18-24, and 31 under 35 U.S.C. § 103(a), as being unpatentable over U.S. Patent Publication No. 2003/0077609 A1 to Jakobsen *et al.* (hereinafter "Jakobsen *et al.*) in view of the journal article to Cregan *et al.* (*Theor. Appl. Genet.* 1999, 98: 919-928, hereinafter referred to as "Cregan *et al.*"); the publication of Sambrook *et al.* (Molecular Cloning: A Laboratory Manual 2001, New York: Cold Spring Harbor Laboratory, Vol. 2; 11.35 and 11.98-11.106, hereinafter referred to as "Sambrook *et al.*"); and the publication of Brown (Genomes 1999, New York: John Wiley & Sons, Inc., pp. 18-23 and 136-137, hereinafter referred to as "Brown").

The Patent Office contends that the 37 C.F.R. § 1.131 Declaration submitted with the November 27, 2004 Amendment is defective, thus maintaining the 35 U.S.C. § 103(a) rejection.

Applicants have amended claim 11 to independent form. No new matter has been added by way of the amendment.

Applicants have amended claim 31 to more particularly claim the presently disclosed subject matter. Support for the amendment can be found throughout the

specification as filed, particularly at page 5, lines 5-8. No new matter has been added by way of the amendment.

Restriction and Election of Species

Applicants submit that claim 31 has been amended to more accurately read on the elected species. The Patent Office contends that the elected species recites "all the nucleotides are LNA," but that claim 31 recites that only the first G is an LNA.

As amended, claim 31 recites that the target simple sequence repeat is –5'-$(CA)_6$ –3', wherein the modified oligonucleotide conjugate comprises 3 biotinylated $(GT)_6$-5' bicyclic structures, wherein the LNAs occur at least on the first G, and wherein the target source is a plasmid library.

Applicants submit that the phrase "wherein the LNAs occur at least on the first G" indicates that the first G comprises an LNA and does not mandate any characteristics for the remaining nucleotides. Thus, a modified oligonucleotide wherein all the nucleotides are LNA is encompassed by the scope of claim 31 wherein at least the modified oligonucleotide conjugate comprises bicyclic structures and the first G is an LNA. As such, applicants respectfully submit that claim 31 reads on the elected species.

Applicants submit that support for the amendment can be found throughout the specification as filed, particularly on page 5, lines 5-8. Applicants further submit that no new matter has been added by way of the amendment to claim 31.

Therefore, applicants respectfully request that the Patent Office reinstate the pending status of claim 31.

Response to the Objection to the 37 C.F.R. § 1.131 Declaration

The Examiner contends that the 37 C.F.R. § 1.131 Declaration submitted November 17, 2004 with Amendment A is defective. First, the Patent Office asserts that the declaration is defective because it does not contain a signature from all of the inventors as required by MPEP § 715.04. Second, the Patent Office asserts that the declaration is lacking an averment that the invention was made in the United States, a NAFTA country, or a WTO country. Third, the Patent Office contends that applicants have not met the burden of explaining how the laboratory notebook shows proof of acts amounting to conception, diligence and reduction to practice. Fourth, the Patent Office asserts that not enough facts and/or evidence to corroborate the priority date are set forth in the Declaration. Fifth, the Patent Office contends that the notebook pages are not commensurate in scope with the claims.

After careful consideration of the instant rejection and the Patent Office basis therefore, applicants respectfully traverse the objection and submit the following remarks.

First, submitted herewith is a new Declaration under 37 CFR § 1.131, which includes signatures from both inventors.

Next, applicants respectfully submit that the enclosed Declaration precisely provides explanation as to proof of acts amounting to conception, diligence and reduction to practice. For example, applicants point to the statements presented

within the Declaration, as well as the data provided in Exhibits A and B. The Declaration also states that the inventive activity occurred in the United States.

Further, the Declaration sets forth additional facts and/or evidence to corroborate completion of the invention before the particular date. For example, applicants point to the statements presented within the Declaration, as well as the data provided in Exhibits A and B. Exhibit B provides chromatographs of sequence data from nucleic acids comprising SSRs captured using the modified oligonucleotide conjugates of the claimed subject matter, thereby proving completion of the claimed invention.

Applicants respectfully submit that the Declaration and data provided in Exhibits A and B are commensurate in scope with the pending claims. Under MPEP § 715.03, a cited reference applied against generic claims may be antedated by a declaration under 37 C.F.R. § 1.131 showing completion of the invention of only a single species within the genus prior to the effective date of the reference. Further, even assuming *arguendo* the data provided in the present Declaration is insufficient to support the entire claimed genus, a 37 C.F.R. § 131 declaration need only show prior invention of so much of the claimed subject matter as is disclosed by the reference. *In re Stempel,* 241 F. 2d 755, 113 U.S.P.Q. 77 (C.C.P.A 1957).

In Stempel, the court held that a declaration provided properly antedated the reference, stating:

> all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference.

Id. at 759-60, 113 U.S.P.Q. at 81; se also *In re Stryher*, 435 F. 2d 1340, 1341, 168 U.S.P.Q. 372, 373 (C.C.P.A. 1971) (applying the principle that a Declaration under 37 C.F.R. § 131 need only show prior invention of as much as taught by the reference).

The Examiner asserts that Jakobsen *et al.* provide one or more modified oligonucleotide conjugates, each comprising at least one locked nucleic acid and a linking molecule. Assuming arguendo that the Patent Office assertion is correct, at best, Jakobsen *et al.* only teach the use of biotin linked to an LNA. See Jakobsen *et al.* at page 7, Example 2. See also paragraph 76 and paragraphs 53-63 and the present Official Action at page 5. Therefore, applicants submit the present declaration is sufficient to antedate Jakobsen *et al.* Consequently, applicants respectfully submit that the attached Declaration establishes that the inventive subject matter of the currently pending claims was invented prior to the earliest effective priority date of Jakobsen *et al.*, which is March 25, 2001.

The data set forth on the first page of Exhibit A of the Declaration is a reproduction of p. 146 of a notebook entry entitled "New LNA Oligos," which records experimental conditions related to capturing specific target nucleotide sequences utilizing locked nucleic acids (LNAs) and further including characterizations of the LNAs and reagent quantities and conditions used in the experiments. Specifically, the first page of Exhibit A describes one or more modified oligonucleotide conjugates comprising at least one LNA and a linking molecule. The modified oligonucleotide referred to as "Torrey-2" comprises the listed sequence of $(GC)_6$, with the LNA residues are shown in bold. The linking molecule used for Torrey-2 was biotin.

The second page of Exhibit A is a reproduction of p. 147 of a notebook entry entitled "LNA Capture That Worked," which records further experimental conditions and reagents related to capturing specific target nucleotide sequences utilizing LNAs and results of an experiment. The second page of Exhibit A describes incubating a sample of nucleic acids with the LNA conjugate to thereby form one or more hybridized duplexes, wherein each duplex comprises a target simple sequence repeat ("SSR") portion and an LNA conjugate. The specific experimental conditions labeled "CN" and notated with a box are labeled as "WORKED." This comment is indicative of the successful capture of specific target nucleotide sequences utilizing an LNA, as recited in the pending claims. Particularly, the boxed data on page 147 indicates that 2.5μl of tomato library DNA was incubated with Torrey-2 LNA conjugate and Buffer C to form a hybridized duplex.

Further, the third page of Exhibit A is a reproduction of p. 150 of a notebook entry entitled "LNA Capture Protocol" and describes the protocol used to acquire the dates set forth on the other pages, wherein hybridized duplexes are contacted with a linking source so that the linking molecule forms a bond with the linking source. Specifically, the protocol recites that the biotinylated LNAs are contacted with streptavidin-coated magnetic beads and incubated to allow the biotin to form a bond with the streptavidin-coated beads. The protocol further recites that the hybridized duplexes are then separated from the sample of nucleic acids by extracting the linking source from the sample, followed by a washing step and an incubating step so that the target SSRs dissociate from the LNA conjugates and the magnetic beads.

Specifically, the protocol recites that the magnetic beads are separated from the sample of nucleic acids by use of a magnet, the beads washed eight times in Buffer C, and incubated in Buffer E in order to separate the SSRs from the beads. (This step is also recited on page 147 of the laboratory notebook provided on the second page of Exhibit A: "90°C in 150µl Buffer E – 20 min.") Next, the protocol recites that the SSRs are ethanol precipitated overnight, and purified using a PCR purification kit. Finally, the protocol recites that Life Technologies DH12S cells were transformed with the captured SSR DNA, grown overnight, the colonies picked, and stored at a temperature of -80°C for sequencing.

Finally, Exhibit B is an exact reproduction of the results of sequence data chromatographs resulting from the experiments discussed above and provide in Exhibit A. Page 147 of the laboratory notebook provided in the second page of Exhibit A recites that the experiment worked, and points to plate T2NC01. The sequence data of Exhibit B verifies that the SSRs were recovered and that the experiment was successful. For example, wells E04 and F09 of plate T2NC01 were sequenced and the SSR $(CA)_6$ was discovered at bases 221-232 and 131-142, respectively. This particular sequence data is provided herein in Exhibit B, and the SSRs are underlined for clarity.

Response to the Claim Rejection Under 35 U.S.C. § 103(a)

The Patent Office has rejected claims 1-8, 12-15, 18-24, and 31 under 35 U.S.C. § 103(a) as being unpatentable over Jakobsen *et al.* in view of Cregan *et al.* and Sambrook *et al.* and Brown.

Regarding independent claims 1 and 24, the Patent Office contends that Jakobsen *et al.* discloses methods of using modified LNAs for the isolation, purification, amplification, detection, identification, quantification, or capture of nucleic acids including applications in gene mapping and/or genotyping which reads on the elected invention. See Official Action at p. 5-6.

However, the Patent Office concedes that Jakobsen *et al.* does not teach or suggest utilizing LNAs in a method for capturing target simple sequence repeats (SSR), as recited in independent claims 1 and 24.

The Patent Office asserts that Cregan *et al.*, Sambrook *et al.*, and Brown teach the use of SSRs as target molecules, and that it would have been obvious to one of skill in the art to combine the teachings of Jakobsen et al. with Cregan et al., Sambrook et al., and Brown to render the invention as recited in Claims 1 and 24 obvious.

In response to the 35 U.S.C. § 103(a) rejection, applicants submit herewith a new Declaration under 37 C.F.R. § 1.131, including Exhibits A and B. As discussed above, applicants respectfully submit that the attached Declaration and Exhibits establish that the inventive subject matter of the currently pending claims was

invented prior to the earliest effective priority date of Jakobsen *et al.*, which is March 25, 2001. Consequently, it is respectfully submitted that Jakobsen *et al.* cannot properly be relied upon as a prior art reference against the presently pending claims.

To establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art references when combined. See *In re* Royka 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The Patent Office relies upon Jakobsen *et al.* as a reference to teach using modified LNAs for the capture of nucleic acids. None of the remaining references Cregan *et al.*, Sambrook *et al.*, and/or Brown, teach, either alone or in combination, the use of LNAs for the capture of target SSRs. As such, applicants respectfully submit that none of the references cited by the Patent Office specifically teach or suggest all the claim limitations of either independent claims 1 or 24. As such, applicants submit that claims 1 and 24 are patentably distinguished over Cregan *et al.*, Sambrook *et al.*, and/or Brown either alone or in combination. Applicants therefore respectfully request that the rejection of independent claims 1 and 24 based on the cited references under 35 U.S.C. § 103(a) be withdrawn at this time.

Applicants respectfully submit that claims 2-8, 12-15, 18-23, and 31 depend either directly or indirectly from independent claims 1 or 24. As such, applicants submit that claims 1-8, 12-15, 18-24, and 31 are patentably distinct over the cited references. Therefore, applicants respectfully request that the rejection of independent claims 1-8, 12-15, 18-24, and 31 under 35 U.S.C. § 103(a) be withdrawn at this time.

Claim Objection

Claim 11 has been objected to as depending from a rejected base claim. The Patent Office asserts that claim 11 would be allowable if rewritten in independent form including all of the claim limitations of the base claims and any intervening claims.

Applicants respectfully submit that claim 11 has been amended to independent form by incorporating all of the claim limitations of independent claim 1 into claim 11. Applicants further submit that no new matter has been added by way of the amendment. Therefore, applicants respectfully request that the instant objection to claim 11 be withdrawn at this time.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

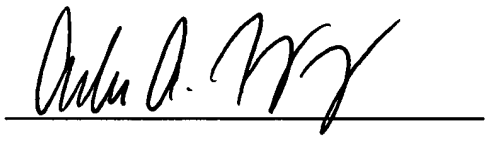
DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

Date: 10/07/2005

By: 

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